Mantle Cell Lymphoma with Diffuse Gastrointestinal Tract Involvement: A Case Report

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Abstract

Gastrointestinal tract mantle cell lymphoma accounts for only approximately 1% to 2% of non-Hodgkin lymphomas. Multiple lymphomatous polyposis is an uncommon disease entity that is regarded as the intestinal form of mantle cell lymphoma. We present here a case of mantle cell lymphoma with peculiar endoscopic presentations in the stomach and colon in a 70 year-old woman. She suffered from abdominal pain, progressive abdominal fullness, and body weight loss of 11 kilograms within 6 months. Big polypoid masses with ulcerations were found at the fundus and high body of the stomach by endoscopy and at the cecal area by colonoscopy. Biopsies from both sites confirmed the diagnosis of mantle cell lymphoma. Computer tomography of the abdomen revealed diffuse wall thickening involving the gastric fundus, high body, antrum, duodenum and proximal ascending colon with extensive mesentery lymph node enlargement. She received one cycle of cyclophosphamide, vincristine and prednisone(COP) followed by seven cycles of rituximab plus cyclophosphamide and prednisone, which resulted in significant tumor regression and prompt symptomatic palliation.（J Intern Med Taiwan 2009; 20: 555-560）

Key Words：Mantle cell lymphoma, Non-Hodgkin lymphomas, Multiple lymphomatous polyposis, Rare endoscopic presentations

Introduction

Primary non-Hodgkin's lymphoma (NHL) of the gastrointestinal tract is the most common extranodal NHL and accounts for 4%-20% of all NHL[1]. Mantle cell lymphoma (MCL) comprises 2.5%-7% of all NHL[2]. Gastrointestinal tract involvement occurred in 20% of MCL, which is commonly manifested as numerous, small, spherical, or hemispherical polyps, termed multiple lymphomatous polyposis (MLP)[1,3]. Hereby we report a case of mantle cell lymphoma with diffuse gastrointestinal tract involvement, including stomach, ileum, colon, mesentery lymph nodes and nasopharynx with emphasizing on its endoscopic features.

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Case Report

A 70-year-old female patient presenting with epigastric pain, progressive abdomen fullness and body weight loss of 11 kilograms in the past 6 months. She denied any systemic diseases history, except gastric ulcer diagnosed six months ago. Endoscopic examination revealed ulcerated polypoid lesions arising from enlarged folds at the fundus and high body of the stomach (Fig. 1). Under the tentative diagnosis of malignant gastric tumor, biopsy was taken, which showed the features of diffuse large B cell lymphoma in histology. Computer tomography of the abdomen revealed diffuse wall thickening involving the gastric fundus and high body, antrum and duodenum and proximal ascending colon with extensive mesentery lymph node enlargement (Fig. 2). Subsequent colonfiberoscopic examination revealed a large ulcerated polypoid mass at the cecum, while most of the rest part of the colon were covered with multiple small polypoid lesions (Fig. 3 and 4). Biopsy specimen taken from the cecum lesion also showed diffuse large B cell lymphoma with positive staining for CD20, CD 5 and cyclin D1 in immunohistochemical study (Fig. 5A-D).

Laboratory data were as follows: white blood count: 7400 / μL (3500~11000 / μL), hemoglobin: 10.8 g/dL (12~16 g/dL), hematocrit: 30.6% (36~46%), platelet count: 210 x 10^3/CM^2 (150~400 x 10^3 /CM^2), lymphocyte: 4% (20~56%), abnormal lymphocyte: 8%(0%), serum albumin: 3 gm/dL(3~5 gm/dL), calcium: 7.8 mg/dL (7.9~9.9 mg/dL), phosphate: 3.9(2.5~4.5 mg/dL), uric acid: 5.4 mg/dL (2.7~8.3 mg/dL), creatinine: 0.8 mg/dL (0.44~1.03 mg/dL), sodium: 143 mmol/L (134~148 mmol/L), potassium: 3.8 mmol/L (3~4.8 mmol/L). Further examinations documented bone marrow, peripheral blood and nasopharyngeal involvement by histological examination of biopsy specimen and blood smear, thus according to the Ann Arbor staging system[4], the final diagnosis was stage IVEB MCL. The patient received one cycle of cyclophosphamide, vincristine, and prednisone, which was then shifted to rituximab plus cyclophosphamide and prednisone because of vincristine-associated neurotoxicity and the approval of rituximab by National Health Insurance Bureau for additional seven cycles. After the 10 months of treatment, follow-up abdomen computer tomography revealed remarkable regression of her bowel loop thickening

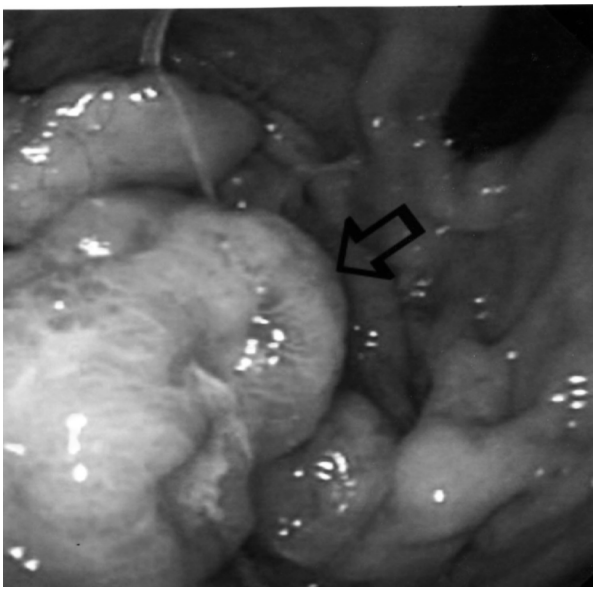

Fig.1. MCL involved stomach: Endoscopy revealed ulcerated polypoid lesions arising from enlarged folds at fundus and high body of the stomach(arrow).

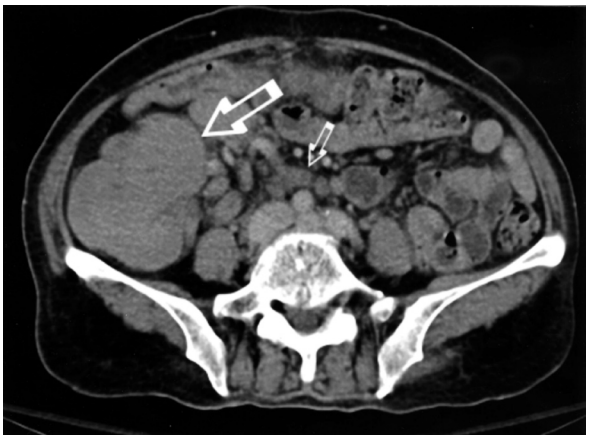

Fig.2. Abdominal computer tomography revealed extensive gastrointestinal tract involvement, mesenteric lymph nodes(arrows).

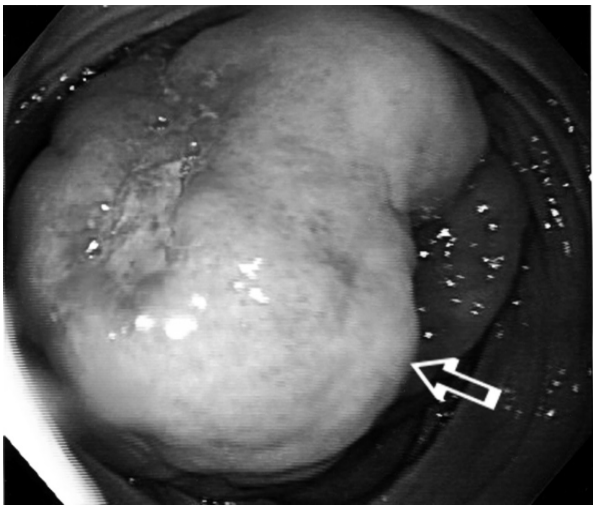

Fig.3. Mantle cell lymphoma with cecal involvement: Colonoscopy revealed big solitary polypoid lesion with ulcerations at the cecal area(arrow).

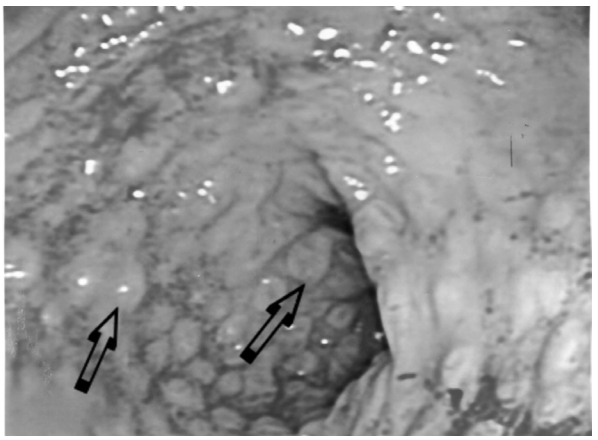

Fig.4. The characteristic colonoscopic features of MCL with small polypoid mucosa over the whole of the colon(arrow).

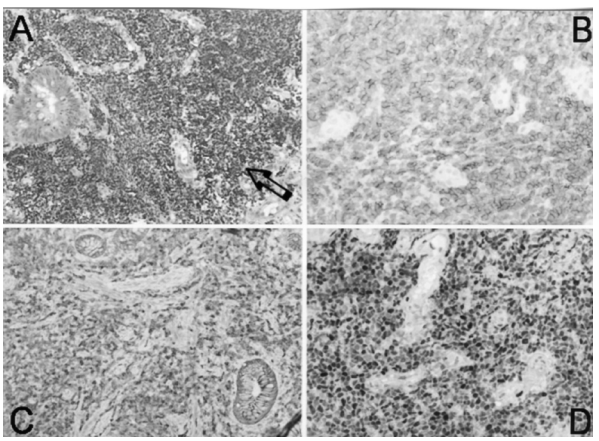

Fig.5. Biopsy specimen from the cecum, H&E stain x 100(A)(arrow), Immunohistochemical stain showed positive CD 20 (B), CD 5(C), and Cyclin D1 (D).

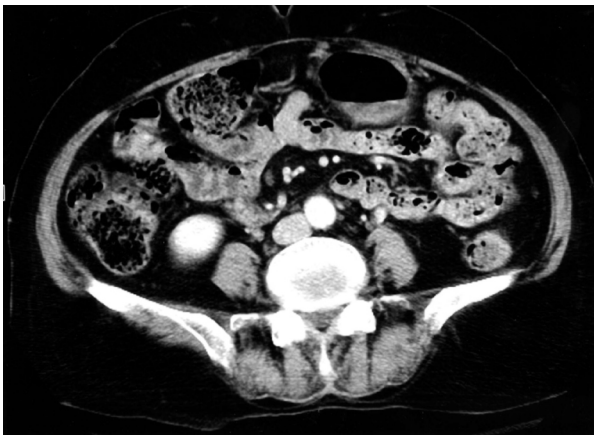

Fig.6. Computer tomography of the abdomen which showed marked regression of MCL which involved gastrointestinal tract and mesenteric lymph nodes.

and disappearance of most enlarged mesentery lymph nodes that was associated with amelioration of symptoms at time of writing (Fig. 6).

Discussion

Most of primary GI NHL presented with single lesion[5]. which more commonly involved the stomach and small intestine, while esophageal and colorectal lymphomas are relatively rare[1] MCL is an uncommon entity of primary GI NHL with distinctive morphological, immunophenotypic, and cytogenetic features[6,7]. In a retrospective study, Morton et al[8] reported that the most common histopathological types among 175 primary gastrointestinal tract lymphoma cases were diffuse large-cell subtype (41%), and mucosa-associated lymphoid tissue type(35%), while only 2% of the patients were classified as having MLP[8]. Similarly, Kohno et al[9] reported that only 4.9% of 143 primary small and large intestines lymphomas were belonged to MCL. Clinically patients with MCL were typically elder adults with a male predominance and presented with advanced stage of diseases, i.e. up to 80% of them have extranodal sites

involvement, including the bone marrow, spleen and gastrointestinal tract[10,11]. The incidence of gastrointestinal tract involvement ranged from 10% to 28% in various series[12]. The typical endoscopic feature of early stage MCL is the appearance of MLP with numerous, small, spherical, or hemispherical polyps, as what was seen in most part of the colon in our patient. Although the pictures are generally different from early stage ileocolonic MALT lymphoma, which usually presented as solitary or multiple mucosa protrusions, but the gross appearance of the two disease entities can be overlapping[3]. On the other hand, the endoscopic features of advanced MCL with GI tract involvement has been classified into three types: 1.elevation type, 2.diffuse infiltration type and 3.ulceration type, which are commonly associated with extra-intestinal involvement, i.e. intra-abdominal lymphadenopathy and/or bone marrow disease. Recently, Romaguera et al[13] reported that the abnormal endoscopic findings of upper and lower gastrointestinal tract in 71 MCL patients were as following: inflammation (29.2 versus 0%); nodules and polyps (50% versus 92.6%); ulcer (12.5% versus 3.7%); thickness (4.2% versus 3.7%); and mass (4.2% versus 0%), respectively. More importantly, Romaguear et al[13] found that microscopic involvement in grossly normal mucosa was a common event in MCL patients. But such microscopic dose not significantly affect the clinical outcomes of the patients.

The presence of huge ulcerated, polypoid masses at both high body and fundus of the stomach and/or the cecum in our patient is not a typical finding in advanced MCL[14]. However, the diagnosis was finally made based on typical Immunohistochemical findings. MCL cells are know to express B-cell markers including CD19, CD20, CD22, as well as T-cell marker of CD5, and cyclin D1[15]. The classic cytogenetic t (11;14)(q13;q32) translocation with secondary overexpression of cyclin D1 protein, due to the translocation of the cyclin-D1 gene (on 11q13) to the promoter of the immunoglobulin heavy chain (on 14q32), are diagnostic for MCL[10,16]. Current standard of care for patients with disseminated low-grade NHL is anti-CD20 antibody, rituximab, in combination with systemic chemotherapy. Patients with massive splenomegaly may benefit from splenectomy to relieve symptoms and improve blood counts before systemic chemotherapy[17]. In MCL, the tumor response rate after rituximab monotherapy was around 30%, which might increase to above 90% while in combination with an anthracyclin-containing regimen[18,19]. Therefore, rituximab is generally given in combination with standard chemotherapy regimens with or without stem cell transplantation for advanced MCL. In one recent randomization study, Dreyling et al[20] showed that autologous stem-cell transplantation following inductional CHOP chemotherapy, although significantly prolonged progression-free survival, but did not improve overall survival of patients with MCL. The findings suggested aggressive chemotherapy might not provide additional survival benefit for this low-grade NHL as compared with less aggressive regimen. Of our patient, for her advanced age and poor general condition, she was initially treated with doxorubicin-sparing COP, which was then shifted to CP plus rituximab due to vincristine-associated toxicity. This mild regimen achieved a remarkable tumor regression along with a significant symptomatic palliation. In general, patients with MCL tended to have a poorer outcome than those with other low-grade NHL(i.e. follicular lymphoma and mucosa-associated lymphoid tissue type lymphoma), with a 5-year survival rate of 11%[21]. However, a variety of new agents including bortezomib, are the first drug specifically approved for this lymphoma subtype, and the others, such as bendamusine, mTOR inhibitors, and lenalidomide, have also shown clear single-agent activity against

MCL[22]. These agents may shed light on the future management of this difficult tumor.

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廣泛胃腸道侵犯之被套細胞淋巴瘤 (mantle cell lymphoma)：一個病例報告

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摘　要

被套細胞淋巴瘤(mantle cell lymphoma)占了非何杰金氏淋巴瘤(non-Hodgkin lymphoma)的百分之五到十，而其中約有百分之二十侵犯到胃腸道。多發性淋巴息肉症(multiple lymphomatous polyposis)是一種少見的疾病。一般認爲它是被套細胞淋巴瘤的一種腸道表現。其表徵以多發性，小息肉樣病灶爲主而同時併有胃與大腸的大息肉樣腫瘤者更爲罕見。我們報告一個罹患的70歲女性主訴腹痛，腹脹與六個月之內體重減輕超過十一公斤。胃鏡發現胃的底部和大腸鏡發現盲腸處都有表面潰瘍的大息肉樣的腫瘤，兩者切片之後確定都是被套細胞淋巴瘤。腹部電腦斷層檢查所見爲廣泛性的胃腸壁增厚，腸繫膜淋巴結之侵犯。患者接受了三次的化學治療包括COP (cyclophosphamide, vincristine, and prednisone)和六次的CP (cyclophosphamide, prednisone)而且搭配七次的Rituximab的治療並獲得顯著的治療效果。胃腸道被套細胞淋巴瘤的內視鏡表徵主要以多發性淋巴息肉症表現。偶爾也有單一的大息肉樣腫瘤病灶的病例，但同時併有多發性胃與大腸的大息肉樣腫瘤者相當罕見。